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~~correcting the model to substantially conform [to the physiology] a specific arterial anatomy and physiology [of the region] of the living subject;~~

~~perturbing the corrected model; and~~

~~determining a set of flow and pressure changes occurring within the corrected model as a result of the perturbation.~~

#### R E M A R K S

1. Claims 1-50 are pending in this application. Claims 1-4, 12-15, 23-32, 40-42 and 50 have been provisionally rejected under 35 U.S.C. §101 as claiming the same invention as claims 1-4, 12-15, 23-32, 40-42 and 50 of copending Application No. 09/243,870. Claims 5-11, 16-22, 33-39 and 43-49 have been provisionally rejected under the judicially created doctrine of double patenting over claims 5-11, 16-22, 33-39 and 43-49 copending Application No. 09/243,870. Claims 1-50 have been rejected under 35 U.S.C. §102(f) based upon the assertion that the applicant did not invent the claimed subject matter. Claims 1-50 have been rejected under 35 U.S.C. §102(b) as being anticipated by Karplus et al. Claims 1-50 have been rejected under 35 U.S.C. §103(a) as being obvious over Foutrakis. After a careful review of the claims (as amended), it is believed that the rejections are in error and the rejections, therefore, are traversed.

2. Claims 1-4, 12-15, 23-32, 40-42 and 50 have been provisionally rejected as claiming the same invention as claims 1-4, 12-15, 23-32, 40-42 and 50 of copending Application No. 09/243,870. In response, the claims have been amended to clarify the differences between the two applications.

3. Claims 5-11, 16-22, 33-39 and 43-49 have been provisionally rejected under the judicially created doctrine of double patenting over claims 5-11, 16-22, 33-39 and 43-49 copending Application No. 09/243,870. However, the rejection of these dependent claims is obviated by the amendment of the base claims upon which these claims depend.

4. Claims 1-50 have been rejected under 35 U.S.C. §102(f) based upon the assertion that the applicant did not invent the claimed subject matter. However, it is well-established that an examiner is not allowed to speculate as to inventorship. The party or parties executing the declaration are presumed to be the inventors. Driscoll v. Cebalo, 5 USPQ2d, 1477, 1481 (Bd. Pat. Int., 1982). Since the named inventors have all attested that they are "original, first and joint inventor . . . of the subject matter which is claimed", the rejection is improper and should be withdrawn.

5. Claims 1-50 have been rejected as being anticipated by Karplus et al. In particular, the Examiner asserts that:

"Karplus . . . discloses a method and apparatus for modeling circulation of cerebrovascular systems of specific patients using MRI scans of the patient's brain and simulating the circulation parameters to model aneurysms. The simulator is used to assist and train medical personnel in planning treatments to the patient before actually performing the procedure".

It is noted first, in this regard, that Karplus is drawn to the modeling of aneurysms, not arterial circulatory systems. As explicitly stated by Karplus "The region occupied by the aneurysm in each slice is identified and enlarged so that the display is focused on the aneurysm, while the rest of the image is discarded" (Karplus, p. 38, par. 3.1). Since the rest of the image is discarded, Karplus is clearly limited to the modeling of aneurysms.

In contrast to Karplus, the claims of the invention are drawn to method steps of (and apparatus for) "developing a pressure and flow model of an arterial circulatory system for living subjects in general". Under illustrated embodiments of the invention, "A baseline vessel network 100 is used in the current model, including the Circle of Willis, ophthalmic arteries and other natural anastomoses" (Specification, p. 37, lines 22-24). Since Karplus is limited to aneurysms of individual blood vessels, it is clearly different than the claimed invention.

Further, the claimed invention is limited to specific method steps of (and apparatus for) and "correcting the model of the circulatory system to substantially conform to a specific arterial anatomy and physiology of the living subject". Since Karplus is limited to aneurysms and uses MRI images of individual patients (Karplus, p. 37, §3.1), there is no "pressure and flow model of an arterial circulatory system, in general" and certainly no correction of the model to conform to the specific arterial anatomy or physiology of the living subject.

Further, "The process of the present invention creates a virtual replica of the environs of the Circle of Willis or other vascular networks within the human body and computes the blood flow in this associated network" (Specification, p. 23, lines 22-26). "The modeling program also allows analysis and simulation of flow and pressure within the cerebrum and/or other organs under the condition of a selected blood flow perturbation (e.g., a cerebral aneurysm, stenosis, bypass, other cerebrovascular disease, trauma etc.)" (Specification, p. 23, lines 26-31).

To summarize, since Karplus is limited to aneurysms of individual blood vessels using MRI images of specific patients, it clearly does not teach method steps of (or apparatus for) "developing a model of an arterial circulatory system for living subjects, in general" or "correcting the model of the circulatory system to substantially conform to a specific arterial anatomy

and physiology of the living subject". Since Karplus is not directed to an arterial circulatory system, it certainly doesn't teach of the method step of (or apparatus for) "calculating a flow . . . based upon the corrected model" or "calculating a flow . . . based upon a selected flow perturbation". Since Karplus does not do exactly the same thing in exactly the same way, the rejection is believed to be improper. Since the rejection is improper, it should be withdrawn.

6. Claims 1-50 have been rejected as being obvious over Foutrakis. In particular, the Examiner asserts that the three Foutrakis

"articles are subtopics to the subject of modeling and simulating circulation of blood to the brain to analyze effects of blood flow in aneurysm formation. All three of these articles combined teaches modeling the blood vessels of the brain using MRI images of patients and simulating blood flow characteristics in the brain as recited in the above-identified claims".

In is noted first that the modeling of aneurysms of individual blood vessels is clearly different than modeling an arterial circulation systems. Further, even when taken together, it is not believed that the Foutrakis articles contain the specific limitations of the claimed invention.

For example, the first Foutrakis article (i.e., "Construction of 3-D Intracranial Arterial Meshes from Magnetic Resonance Angiography") fails to teach or suggest the method steps of (or apparatus for) "developing a pressure and flow model

of an arterial circulatory system for living subjects in general" or "correcting the model of the circulatory system to substantially conform to a specific arterial anatomy and physiology of the living subject". Under illustrated embodiments of the invention "A baseline vessel network 100 is used in the current model, including the Circle of Willis, ophthalmic arteries and other natural anastomoses" (Specification, p. 37, lines 22-24).

In contrast, the first Foutrakis article explicitly states that "Herein, we introduce an efficient method to accurately develop realistic 3-D computational meshes of human intracranial arteries and aneurysms from serial MRA images" (first Foutrakis article, Abstract). The computational meshes are computed by segmenting greyscale images, extracting arterial contours, stacking arterial contours and computing cubic splines to effect a smooth integration in the axial direction to provide a set of points defining the 3-D arterial surface geometry (first Foutrakis article, Abstract). The creation of 3-D computational meshes, defined by a 3-D arterial surface geometry, is clearly different than the modeled system of the claimed invention.

For example, "The computer model is a one-dimensional, explicit, finite difference algorithm based on a conservation of mass equation, a Navier-Stokes momentum equation, and an equation of state relating local pressure to local size of artery applied at each vessel segment (Specification, p. 36, lines 9-13). A

pressure and flow model that may be characterized by a one-dimensional, explicit, finite difference algorithm is not the same (or equivalent to) the Foutrakis 3-D mesh which simply defines a 3-D arterial surface geometry.

Further, "The computer simulation system 10 for cerebral circulation employs the outputs from both the vessel extraction system and the three-dimensional phase contrast MR flow measurement system to calibrate, customize and drive the cerebral circulation model" (Specification, p. 35, lines 23-27).

In contrast, the 3-D computational meshes of the first Foutrakis article are based upon "the raw (MRA) image data of an adult human subject" (first Foutrakis article, Introduction). Basing a 3-D computational mesh upon raw MRI data of a single human subject is certainly not the same as "developing a pressure and flow model of an arterial circulatory system for living subjects in general". Further, since the 3-D computational meshes are based upon a single subject there would be no need for "correcting the model of the circulatory system to substantially conform to a specific arterial anatomy and physiology of the living subject".

The first Foutrakis articles states (Abstract) that "The 3-D volume mesh . . . will be used to develop patient-specific computational fluid dynamic models of flow phenomena in intracranial arteries and aneurysms". However, aneurysms are part of a disease pathology that would not be associated with a

pressure and flow model of living subjects in general. Further, the reference clearly refers to the fluid dynamic models prospectively, thereby putting the reader on notice that such models are merely an objective of the research, not a result.

The second Foutrakis article (i.e., "Efficient Segmentation and 3-D Reconstruction of Complex Vascular Structures from Magnetic Resonance Angiography Imaging Data") suffer from many of the same deficiencies as the first Foutrakis article. For example, the second Foutrakis article is also limited to the creation of an "accurate three-dimensional representation of the intracranial arterial network" (second Foutrakis article, Abstract). The second Foutrakis article illustrates "The resulting three-dimensional volume-rendered images of the Circle of Willis for two different patients" (second Foutrakis article, Abstract).

Since the second Foutrakis article is drawn to a three-dimensional illustrations of the Circle of Willis for two different patients, the article does not teach or suggest the method step of (or apparatus for) "developing a pressure and flow model of an arterial circulatory system for living subjects in general", as such terms are used under the invention. This is true for the same reason that the first Foutrakis article does not teach or suggest this claim element. Further, since the three-dimensional images are created from the "raw MRA data" (Foutrakis, FIG. 1) of each patient, there would be no need for

"correcting the model of the circulatory system to substantially conform to a specific arterial anatomy and physiology of the living subject".

The third Foutrakis article (i.e., Finite Element Modeling of Intracranial Arterial Blood Flow and Saccular Aneurysm Formation") is limited to aneurysms. More specifically, the third Foutrakis article explicitly states that "various finite element models will be presented describing four distinct stages of aneurysmal development . . . For each model, a description of the finite element mesh, numerical solution procedures and results are presented. This paper presents the simulation and analysis of saccular intracranial aneurysm formation as well as surgical approaches to its management" (third Foutrakis article, Abstract). FIGs. 1-12 provide a pictorial description of the finite element meshes and numerical solution procedures of the Foutrakis models showing a single arterial bifurcation in each figure.

Since the finite element meshes and numerical solution procedures of the models of the third Foutrakis article are fully described in terms of a single arterial bifurcation, a person of skill in the art would understand the third Foutrakis article to be limited to a single arterial bifurcation. Since it is limited to a single arterial bifurcation, the third Foutrakis article could not and does not teach or suggest the modeling an arterial circulatory system.

Further, even assuming, *arguendo*, that the third Foutrakis article did teach modeling an arterial circulatory system (which it does not), there is no teaching or suggestion of correcting the Foutrakis model to conform to a specific anatomy and physiology of a living subject. For example, under illustrated embodiments of the invention "The computer simulation system 10 for cerebral circulation employs the outputs from both the vessel extraction system and the three-dimensional phase contrast MR flow measurement system to calibrate, customize and drive the cerebral circulation model" (Specification, p. 35, lines 23-27). Further, "the model of the system 10 is first initialized 202 with initialized pressures and flows at all nodes in all vessels. A cross-sectional area is calculated 202 for all points using the current pressure. The mass balance is determined 204 by calculating pressures at all points . . . A momentum balance may then be determined 210 by calculating the flows at all points" (Specification, p. 37, lines 1-13).

Nowhere within the third Foutrakis article is there any mention of "a vessel extraction system and the three-dimensional phase contrast MR flow measurement system to calibrate, customize and drive the cerebral circulation model". Without such systems (or their equivalent), the third Foutrakis article could not be considered as providing a means for correcting the Foutrakis model to a specific arterial anatomy and physiology of a living subject.

Since the third Foutrakis article is limited to a single arterial bifurcation, it cannot and does not teach or suggest the method step of (or apparatus for) "developing a pressure and flow model of an arterial circulatory system for living subjects in general", as such terms are used under the claimed invention. Further, since it is concerned with the development of aneurysms, it certainly doesn't teach or suggest the method step of (or apparatus for) "correcting the model of the circulatory system to substantially conform to a specific arterial anatomy and physiology of the living subject".

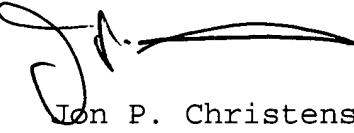
Turning now to the combination of references, for the reasons provided above, the three Foutrakis articles (taken together) also do not teach or suggest, *inter alia*, the method steps of (or apparatus for) "developing a pressure and flow model of an arterial circulatory system for living subjects in general" or of "correcting the model of the circulatory system to substantially conform to a specific arterial anatomy and physiology of the living subject". Since the combination of the three Foutrakis articles fails to teach or suggest each and every claim limitation, the *prima facie* case of obviousness is not believed to have been made as required under MPEP §2143.03. Since the *prima facie* case has not been made, the rejection is improper and should be withdrawn.

6. Allowance of claims 1-50, as now presented, is believed to be in order and such action is earnestly solicited. Should the Examiner be of the opinion that a telephone conference would expedite prosecution of the subject application, he is respectfully requested to telephone applicant's undersigned attorney.

Respectfully submitted,

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